EAST Search History

Ref #	Hits	Search Query	DBs	Default Operator	Plurals	Time Stamp
S1	19372	cystic near2 fibrosis	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/12/22 15:58
S2	16002	(((cationic adj protein) cap) near2 "18") "cap 18" cap-18	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/12/22 15:56
S3	1	S1 same S2	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/12/14 12:42
S4	13	S1 and S2	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/12/14 12:42
S5	19416	cystic near2 fibrosis	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2007/01/03 11:46
S6	61766	(((cationic adj (antimicrobial anti-microbial protein)) cap) near2 "18") "cap 18" cap-18 camp (cathelicidin adj (antimicrobial anti-microbial)) fall-39 fall39 hcap-18 hcap18 hsd26 ll37 (cathelin-related adj antimicrobial) clp cnlp cramp mclp ll-37	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/12/22 16:18
S7	2947	S6 and S5	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/12/22 16:07
S8	43	S7 and (cathelicidin cap18 cap-18 (cap adj "18") fall39 fall-39)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/12/22 16:18
S9	193	S6 with (diagnos$3)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2006/12/22 16:18
S10	8	S9 and (cathelicidin cap18 cap-18 (cap adj "18") fall39 fall-39)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2007/01/03 11:47

EAST Search History

S11	15	bals-r$.in.	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2007/01/03 13:42
S12	61957	(((cationic adj (antimicrobial anti-microbial protein)) cap) near2 "18") "cap 18" cap-18 camp (cathelicidin adj (antimicrobial anti-microbial)) fall-39 fall39 hcap-18 hcap18 hsd26 ll37 (cathelin-related adj antimicrobial) clp cnlp cramp mclp ll-37	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2007/01/03 11:45
S13	19482	cystic near2 fibrosis	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2007/01/03 11:46
S15	608	S12 same (S13 cf)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2007/01/03 11:46
S17	23	S15 and (cathelicidin cap18 cap-18 (cap adj "18") fall39 fall-39 ll37 ll-37)	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2007/01/03 11:47
S18	19482	cystic near2 fibrosis	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2007/01/03 13:42
S19	7	larrick-j$.in. and S18	US-PGPUB; USPAT; EPO; JPO; DERWENT	OR	OFF	2007/01/03 13:42

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NEWS 7	SEP 25	CA(SM)/CAplus(SM) display of CA Lexicon enhanced
NEWS 8	SEP 25	CAS REGISTRY(SM) no longer includes Concord 3D coordinates
NEWS 9	SEP 25	CAS REGISTRY(SM) updated with amino acid codes for pyrrolysine
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NEWS 16	OCT 30	CHEMLIST enhanced with new search and display field
NEWS 17	NOV 03	JAPIO enhanced with IPC 8 features and functionality
NEWS 18	NOV 10	CA/CAplus F-Term thesaurus enhanced
NEWS 19	NOV 10	STN Express with Discover! free maintenance release Version 8.01c now available
NEWS 20	NOV 20	CAS Registry Number crossover limit increased to 300,000 in additional databases
NEWS 21	NOV 20	CA/CAplus to MARPAT accession number crossover limit increased to 50,000
NEWS 22	DEC 01	CAS REGISTRY updated with new ambiguity codes
NEWS 23	DEC 11	CAS REGISTRY chemical nomenclature enhanced
NEWS 24	DEC 14	WPIDS/WPINDEX/WPIX manual codes updated
NEWS 25	DEC 14	GBFULL and FRFULL enhanced with IPC 8 features and functionality
NEWS 26	DEC 18	CA/CAplus pre-1967 chemical substance index entries enhanced with preparation role
NEWS 27	DEC 18	CA/CAplus patent kind codes updated
NEWS 28	DEC 18	MARPAT to CA/CAplus accession number crossover limit increased to 50,000
NEWS 29	DEC 18	MEDLINE updated in preparation for 2007 reload
NEWS 30	DEC 27	CA/CAplus enhanced with more pre-1907 records

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=> s (cathelicidin OR cap18 OR cap-18 OR hcap18 OR hcap-18 OR "cap 18" OR "hcap 18" OR fall39 OR fall-39 OR ll37 OR ll-37 OR "ll-37/hcap-18")
L1 2377 (CATHELICIDIN OR CAP18 OR CAP-18 OR HCAP18 OR HCAP-18 OR "CAP 18" OR "HCAP 18" OR FALL39 OR FALL-39 OR LL37 OR LL-37 OR "LL-37/HCAP-18")

=> s l1 AND ("cystic fibrosis" OR "cystic lung fibrosis")
L2 72 L1 AND ("CYSTIC FIBROSIS" OR "CYSTIC LUNG FIBROSIS")

=> dup rem l2
PROCESSING COMPLETED FOR L2
L3 36 DUP REM L2 (36 DUPLICATES REMOVED)

=> d ibib ed abs l3 1-36

L3 ANSWER 1 OF 36 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2006:670645 BIOSIS
DOCUMENT NUMBER: PREV200600665912
TITLE: Antimicrobial peptides in the airway.
AUTHOR(S): Laubel, D. M.; Yiml, S.; Ryan, L. K.; Kisich, K. O.; Diamond, G. [Reprint Author]
CORPORATE SOURCE: Univ Med and Dent New Jersey, New Jersey Med Sch, Dept Oral Biol, Newark, NJ 07101 USA
gdiamond@umdnj.edu
SOURCE: Shafer, WM [Editor]. Curr. Top. Microbiol. Immunol., (2006) pp. 153-182. Current Topics in Microbiology and Immunology. Publisher: SPRINGER-VERLAG BERLIN, HEIDELBERGER PLATZ 3, D-14197 BERLIN, GERMANY. Series: CURRENT TOPICS IN MICROBIOLOGY AND IMMUNOLOGY.
CODEN: CTMIA3. ISSN: 0070-217X. ISBN: 3-540-29915-7(H).
DOCUMENT TYPE: Book; (Book Chapter)
LANGUAGE: English
ENTRY DATE: Entered STN: 6 Dec 2006

Last Updated on STN: 6 Dec 2006

ED Entered STN: 6 Dec 2006
Last Updated on STN: 6 Dec 2006

AB The airway provides numerous defense mechanisms to prevent microbial colonization by the large numbers of bacteria and viruses present in ambient air. An important component of this defense is the antimicrobial peptides and proteins present in the airway surface fluid (ASF), the mucin-rich fluid covering the respiratory epithelium. These include larger proteins such as lysozyme and lactoferrin, as well as the cationic defensin and cathelicidin peptides. While some of these peptides, such as human beta-defensin (hBD)-1, are present constitutively, others, including hBD2 and -3 are inducible in response to bacterial recognition by Toll-like receptor-mediated pathways. These peptides can act as microbicides in the ASF, but also exhibit other activities, including potent chemotactic activity for cells of the innate and adaptive immune systems, suggesting they play a complex role in the host defense of the airway. Inhibition of antimicrobial peptide activity or gene expression can result in increased susceptibility to infections. This has been observed with cystic fibrosis (CF), where the CF phenotype leads to reduced antimicrobial capacity of peptides in the airway. Pathogenic virulence factors can inhibit defensin gene expression, as can environmental factors such as air pollution. Such an interference can result in infections by airway-specific pathogens including Bordetella bronchiseptica, Mycobacterium tuberculosis, and influenza virus. Research into the modulation of peptide gene expression in animal models, as well as the optimization of peptide-based therapeutics shows promise for the treatment and prevention of airway infectious diseases.

L3 ANSWER 2 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN

ACCESSION NUMBER: 2006:1240995 CAPLUS
TITLE: The antimicrobial peptide cathelicidin interacts with airway mucus
AUTHOR(S): Felgentreff, Kerstin; Beisswenger, Christoph; Griese, Matthias; Gulder, Tanja; Bringmann, Gerhard; Bals, Robert
CORPORATE SOURCE: Department of Internal Medicine, Division for Pulmonary Diseases, Philipps-Universitaet Marburg, Marburg, 35043, Germany
SOURCE: Peptides (New York, NY, United States) (2006), 27(12), 3100-3106
CODEN: PPTDD5; ISSN: 0196-9781
PUBLISHER: Elsevier Inc.
DOCUMENT TYPE: Journal
LANGUAGE: English

ED Entered STN: 28 Nov 2006

AB Antimicrobial peptides (AMPs) and mucins are components of airway secretions and both contribute to the innate host defense system. At neutral pH, AMPs are pos. charged, mucins neg. It was the aim here to test whether these opposite charges result in interactions between AMPs and mucins. The authors measured binding of mucins isolated from porcine gastric mucosa to the cathelicidin LL-37 coated to multiwell plates and found that LL-37 electrostatically interacts with mucins. CD spectra of the peptide revealed the induction of α-helical conformation by mucins. Addition of mucins to solns. of LL-37 decreased the antimicrobial activity of the peptide against Pseudomonas aeruginosa and Streptococcus pneumoniae. The authors then tested whether LL-37 is bound to mucins in airway secretions from human subjects and found that a proportion of the peptide and its propeptide are bound to high mol. weight components. Thus, cationic AMPs interact with anionic mucins in airway secretions. Functions of AMPs are modulated by this interaction.

L3 ANSWER 3 OF 36 MEDLINE on STN DUPLICATE 1

ACCESSION NUMBER: 2006485827 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16909921
TITLE: Antimicrobial peptides in the airway.
AUTHOR: Laube D M; Yim S; Ryan L K; Kisich K O; Diamond G
CORPORATE SOURCE: Department of Oral Biology, UMDNJ-New Jersey Dental School, Newark 07101, USA.
SOURCE: Current topics in microbiology and immunology, (2006) Vol. 306, pp. 153-82. Ref: 156
Journal code: 0110513. ISSN: 0070-217X.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200608
ENTRY DATE: Entered STN: 17 Aug 2006
Last Updated on STN: 1 Sep 2006
Entered Medline: 31 Aug 2006

ED Entered STN: 17 Aug 2006
Last Updated on STN: 1 Sep 2006
Entered Medline: 31 Aug 2006

AB The airway provides numerous defense mechanisms to prevent microbial colonization by the large numbers of bacteria and viruses present in ambient air. An important component of this defense is the antimicrobial peptides and proteins present in the airway surface fluid (ASF), the mucin-rich fluid covering the respiratory epithelium. These include larger proteins such as lysozyme and lactoferrin, as well as the cationic defensin and cathelicidin peptides. While some of these peptides, such as human beta-defensin (hBD)-1, are present constitutively, others, including hBD2 and -3 are inducible in response to bacterial recognition by Toll-like receptor-mediated pathways. These peptides can act as microbicides in the ASF, but also exhibit other activities, including potent chemotactic activity for cells of the innate and adaptive immune systems, suggesting they play a complex role in the host defense of the airway. Inhibition of antimicrobial peptide activity or gene expression can result in increased susceptibility to infections. This has been observed with cystic fibrosis (CF), where the CF phenotype leads to reduced antimicrobial capacity of peptides in the airway. Pathogenic virulence factors can inhibit defensin gene expression, as can environmental factors such as air pollution. Such an interference can result in infections by airway-specific pathogens including Bordetella bronchiseptica, Mycobacterium tuberculosis, and influenza virus. Research into the modulation of peptide gene expression in animal models, as well as the optimization of peptide-based therapeutics shows promise for the treatment and prevention of airway infectious diseases.

L3 ANSWER 4 OF 36 MEDLINE on STN
ACCESSION NUMBER: 2006485824 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16909918
TITLE: Host antimicrobial defence peptides in human disease.
AUTHOR: Agerberth B; Gudmundsson G H
CORPORATE SOURCE: Department of Medical Biochemistry and Biophysics, Karolinska Institutet, Stockholm, Sweden.
SOURCE: Current topics in microbiology and immunology, (2006) Vol. 306, pp. 67-90. Ref: 112
Journal code: 0110513. ISSN: 0070-217X.
PUB. COUNTRY: Germany: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200608
ENTRY DATE: Entered STN: 17 Aug 2006
Last Updated on STN: 1 Sep 2006

Entered Medline: 31 Aug 2006

ED Entered STN: 17 Aug 2006
Last Updated on STN: 1 Sep 2006
Entered Medline: 31 Aug 2006

AB Antimicrobial peptides or host defence peptides are endogenous peptide antibiotics, which have been confirmed as an essential part of the immune system. Apart from direct killing of bacteria, a role for the peptides in antiviral and immunomodulatory functions has recently been claimed. In this chapter we have focused on the host contact with microbes, where these host defence peptides are key players. The interplay with commensals and pathogens in relation to antimicrobial peptide expression is discussed, with specific emphasis on the respiratory and the alimentary systems. A possible novel difference in epithelial interactions between commensals and pathogens is considered in relation to disease.

L3 ANSWER 5 OF 36 MEDLINE on STN DUPLICATE 2

ACCESSION NUMBER: 2005559788 MEDLINE
DOCUMENT NUMBER: PubMed ID: 16236890
TITLE: Sputum cathelicidin, urokinase plasminogen activation system components, and cytokines discriminate cystic fibrosis, COPD, and asthma inflammation.
AUTHOR: Xiao Wei; Hsu Yao-Pi; Ishizaka Akitoshi; Kirikae Teruo; Moss Richard B
CORPORATE SOURCE: Department of Medicine, Shandong University, Jinan, People's Republic of China.
SOURCE: Chest, (2005 Oct) Vol. 128, No. 4, pp. 2316-26. Journal code: 0231335. ISSN: 0012-3692.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 200511
ENTRY DATE: Entered STN: 21 Oct 2005
Last Updated on STN: 16 Dec 2005
Entered Medline: 21 Nov 2005

ED Entered STN: 21 Oct 2005
Last Updated on STN: 16 Dec 2005
Entered Medline: 21 Nov 2005

AB BACKGROUND: Interest in airways inflammatory disease has increasingly focused on innate immunity. We investigated several components of innate immunity in induced sputum of patients with cystic fibrosis (CF), COPD, and asthma, and healthy control subjects. METHODS: Twenty eight patients with mild CF lung disease (age > or = 12 years; FEV1, 74 +/- 3% predicted [mean +/- SE]), 74 adults with COPD (FEV1, 55 +/- 2% of predicted), 34 adults with persistent asthma (FEV1, 66 +/- 2% of predicted), and 44 adult control subjects (FEV1, 85 +/- 1% of predicted) were studied while in stable clinical condition. Levels of sputum interleukin (IL)-8, IL-10, interferon (IFN)-gamma, tumor necrosis factor (TNF)-alpha, human cationic antimicrobial protein 18 (CAP18), urokinase-type plasminogen activator (uPA), uPA receptor (uPAR), and plasminogen activator inhibitor (PAI)-1 were determined. Cell sources were investigated by flow cytometry and immunohistochemistry. Spirometry was performed prior to sputum induction. RESULTS: CF patient sputum showed greatest increase in IL-8 compared to that of patients with COPD and asthma (which were also greater than control subjects), and elevated levels of TNF-alpha and IL-10 compared to other groups. There were no differences in IFN-gamma. CAP18 levels were elevated in CF and COPD patients compared to control subjects, while asthma patients had reduced CAP18 levels. uPA levels were similar but uPAR was elevated in CF and COPD patients more so than in asthma patients, while PAI-1 levels were elevated in all three disease groups. CAP18 localized to neutrophil secondary granules; neutrophils were also sources of IL-8 and PAI-1. CAP18 and PAI-1 negatively correlated with pulmonary function. CONCLUSION: Induced-sputum innate immune factor

levels discriminate inflammatory changes in CF, COPD, and asthma, suggesting potential roles in pathophysiology and as well as providing disease-specific biomarker patterns.

L3 ANSWER 6 OF 36 MEDLINE on STN DUPLICATE 3
ACCESSION NUMBER: 2005145995 IN-PROCESS
DOCUMENT NUMBER: PubMed ID: 15778507
TITLE: Pulmonary defense and the human cathelicidin hCAP-18/LL-37.
AUTHOR: Fahy R J; Wewers M D
CORPORATE SOURCE: Division of Pulmonary and Critical Care Medicine, The Ohio State University Medical Center, Columbus, OH 43210-1252, USA.. fahy-1@medctr.osu.edu
SOURCE: Immunologic research, (2005) Vol. 31, No. 2, pp. 75-89. Ref: 83
Journal code: 8611087. ISSN: 0257-277X.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: NONMEDLINE; IN-PROCESS; NONINDEXED; Priority Journals
ENTRY DATE: Entered STN: 22 Mar 2005
Last Updated on STN: 13 Dec 2006
ED Entered STN: 22 Mar 2005
Last Updated on STN: 13 Dec 2006
AB Antimicrobial peptides form an important component of the innate immune system. The cathelicidin family, a key member of the antimicrobial peptide defenses, has been highly conserved throughout evolution. Though widespread in mammals, there is currently only one identified human example, hCAP-18/LL-37. The cathelicidins have been found to have multiple functions, in addition to their known antimicrobial and lipopolysaccharide-neutralizing effects. As a result, they profoundly affect both innate and adaptive immunity. Currently, antimicrobial peptides are being evaluated as therapeutic drugs in disease states as diverse as oral mucositis, cystic fibrosis, and septic shock. One such peptide, the cathelicidin hCAP-18/LL-37, is reviewed in detail in the context of its role in lung physiology and defense.

L3 ANSWER 7 OF 36 EMBASE
ACCESSION NUMBER: 2005432483 EMBASE
TITLE: Anionic poly(amino acid)s dissolve F-actin and DNA bundles, enhance DNase activity, and reduce the viscosity of cystic fibrosis sputum.
AUTHOR: Tang J.X.; Wen Q.; Bennett A.; Kim B.; Sheils C.A.; Bucki R.; Janmey P.A.
CORPORATE SOURCE: R. Bucki, Dept. of Physiology, Inst. for Medicine and Engineering, Univ. of Pennsylvania, 3340 Smith Walk, Philadelphia, PA 19104, United States. buckirob@mail.med.upenn.edu
SOURCE: American Journal of Physiology - Lung Cellular and Molecular Physiology, (2005) Vol. 289, No. 4 33-4, pp. L599-L605. .
Refs: 30
ISSN: 1040-0605 CODEN: APLPE7
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 002 Physiology
005 General Pathology and Pathological Anatomy
027 Biophysics, Bioengineering and Medical Instrumentation
LANGUAGE: English
SUMMARY LANGUAGE: English

ENTRY DATE: Entered STN: 3 Nov 2005
Last Updated on STN: 3 Nov 2005
ED Entered STN: 3 Nov 2005
Last Updated on STN: 3 Nov 2005
AB Bundles of F-actin and DNA present in the sputum of cystic fibrosis (CF) patients but absent from normal airway fluid contribute to the altered viscoelastic properties of sputum that inhibit clearance of infected airway fluid and exacerbate the pathology of CF. Previous strategies to remove these filamentous aggregates have focused on DNase to enzymatically depolymerize DNA to constituent monomers and gelsolin to sever F-actin to small fragments. The high densities of negative surface charge on DNA and F-actin suggest that the bundles of these filaments, which alone exhibit a strong electrostatic repulsion, may be stabilized by multivalent cations such as histones, antimicrobial peptides, and other positively charged molecules prevalent in airway fluid. This study reports that bundles of DNA or F-actin formed after addition of histone H1 or lysozyme are efficiently dissolved by soluble multivalent anions such as polymeric aspartate or glutamate. Addition of poly-aspartate or poly-glutamate also disperses DNA and actin-containing bundles in CF sputum and lowers the elastic moduli of these samples to levels comparable to those obtained after treatment with DNase I or gelsolin. Addition of poly-aspartic acid also increased DNase activity when added to samples containing DNA bundles formed with histone H1. When added to CF sputum, polyaspartic acid significantly reduced the growth of bacteria, suggesting activation of endogenous antibacterial factors. These findings suggest that soluble multivalent anions have potential alone or in combination with other mucolytic agents to selectively dissociate the large bundles of charged biopolymers that form in CF sputum. Copyright .COPYRGT. 2005 the American Physiological Society.

L3 ANSWER 8 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2004:717880 CAPLUS
DOCUMENT NUMBER: 141:221292
TITLE: Method for evaluating cystic pulmonary fibrosis by measuring CAP18
INVENTOR(S): Moss, Richard B.; Ishizaka, Akitoshi; Kirikae, Teruo
PATENT ASSIGNEE(S): Seikagaku Kogyo Co., Ltd., Japan
SOURCE: Jpn. Kokai Tokkyo Koho, 14 pp.
CODEN: JKXXAF
DOCUMENT TYPE: Patent
LANGUAGE: Japanese
FAMILY ACC. NUM. COUNT: 1
PATENT INFORMATION:

PATENT NO.	KIND	DATE	APPLICATION NO.		DATE
JP 2004245842	A	20040902	JP 2004-36471		20040213
US 2005032117	A1	20050210	US 2004-777683		20040213
PRIORITY APPLN. INFO.:			US 2003-447310P	P	20030214

ED Entered STN: 02 Sep 2004
AB A method is provided for performing the evaluation of cystic pulmonary fibrosis (e.g., seriousness degree, acuteness degree, progress degree) useful for its management with high accuracy, high sensitivity, convenience, rapidity and low cost. Also provided is a kit used for this method. This method for evaluating cystic pulmonary fibrosis comprises at least a step for measuring the quantity of CAP18 in a biol. sample, and relating the measurement result to cystic lung fibrosis. Preferably, the method comprises the following three steps: (1) a step for measuring the quantity of CAP18 in a biol. sample collected from an individual; (2) a step for comparing the quantity of CAP18 measured by the step (1) with the quantity of CAP18 in a control sample; and (3) a step for relating the result obtained at the step (2) to cystic pulmonary fibrosis.

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ACCESSION NUMBER: 2004202600 EMBASE
TITLE: Towards gene therapy for inflammatory and infective pulmonary diseases.
AUTHOR: Simpson A.J.; King J.A.; Thorpe P.H.; McLachlan G.; Sallenave J.-M.
CORPORATE SOURCE: A.J. Simpson, Respiratory Medicine Unit, Rayne Laboratory, MRC Centre for Inflammation Research, Teviot Place, Edinburgh EH8 9AG, United Kingdom. A.J.Simpson@ed.ac.uk
SOURCE: Current Genomics, (2004) Vol. 5, No. 4, pp. 365-383. .
Refs: 195
ISSN: 1389-2029 CODEN: CGUEA8
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 015 Chest Diseases, Thoracic Surgery and Tuberculosis
022 Human Genetics
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
039 Pharmacy
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 10 Jun 2004
Last Updated on STN: 10 Jun 2004
ED Entered STN: 10 Jun 2004
Last Updated on STN: 10 Jun 2004
AB Pneumonia is responsible for unacceptably high mortality rates among specific populations of patients, despite the use of conventional antibiotics and improvements in critical care. New treatments for severe pulmonary infection are therefore required. Manipulation of host defence genes using targeted gene therapy seems a logical strategy for severe pulmonary infection, and several groups have recently demonstrated that therapeutic genes can protect the healthy lung against the subsequent development of experimental pneumonia. This article reviews the problems facing the development of gene therapy for human pneumonia, with particular reference to safety issues and to the physical and biological barriers limiting efficient delivery of therapeutic transgenes to cells in the lung. The strengths and weaknesses of vectors currently available for pulmonary gene therapy are also considered, with emphasis on recent developments relating to adenovirus, adeno-associated virus and non-viral vector systems. Thereafter the specific gene therapy strategies used either to enhance clearance of pneumonia in laboratory animals or to immunise rodents against subsequent pulmonary challenge with human pathogens are discussed and placed in the context of future potential applications to human pneumonia. .COPYRGT. 2004 Bentham Science Publishers Ltd.

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ACCESSION NUMBER: 2004028439 EMBASE
TITLE: Alternatives to conventional vaccines - Mediators of innate immunity.
AUTHOR: Eisen D.P.; Liley H.G.; Minchinton R.M.
CORPORATE SOURCE: D.P. Eisen, Infectious Diseases Unit, Royal Brisbane Hospital, Herston Rd., Herston, QLD 4029, Australia. damon_eisen@health.qld.gov.au
SOURCE: Current Drug Targets, (2004) Vol. 5, No. 1, pp. 89-105. .
Refs: 134
ISSN: 1389-4501 CODEN: CDTUAU
COUNTRY: Netherlands
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 004 Microbiology
025 Hematology
026 Immunology, Serology and Transplantation

030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles

LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 29 Jan 2004
Last Updated on STN: 29 Jan 2004

ED Entered STN: 29 Jan 2004
Last Updated on STN: 29 Jan 2004

AB Vaccines have been described as "weapons of mass protection". The eradication of many diseases is testament to their utility and effectiveness. Nevertheless, many vaccine preventable diseases remain prevalent because of political and economic barriers. Additionally, the effects of immaturity and old age, therapies that incapacitate the adaptive immune system and the multitude of strategies evolved by pathogens to evade immediate or sustained recognition by the mammalian immune system are barriers to the effectiveness of existing vaccines or development of new vaccines. In the front line of defence against the pervasiness of infection are the elements of the innate immune system. Innate immunity is under studied and poorly appreciated. However, in the first days after entry of a pathogen into the body, our entire protective response is dependant upon the various elements of our innate immune repertoire. In spite of its place as our initial defence against infection, attention is only now turning to strategies which enhance or supplement innate immunity. This review examines the need for and potential of innate immune therapies.

L3 ANSWER 11 OF 36 MEDLINE on STN DUPLICATE 4
ACCESSION NUMBER: 2004502231 MEDLINE
DOCUMENT NUMBER: PubMed ID: 15463886
TITLE: Beta-defensins and LL-37 in bronchoalveolar lavage fluid of patients with cystic fibrosis.
AUTHOR: Chen Christiane I-U; Schaller-Bals Susanne; Paul Karl P; Wahn Ulrich; Bals Robert
CORPORATE SOURCE: Department of Pediatric Pneumology and Immunology, Charite, Humboldt-University, Berlin, Germany.
SOURCE: Journal of cystic fibrosis : official journal of the European Cystic Fibrosis Society, (2004 Mar) Vol. 3, No. 1, pp. 45-50.
Journal code: 101128966. ISSN: 1569-1993.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200411
ENTRY DATE: Entered STN: 9 Oct 2004
Last Updated on STN: 19 Dec 2004
Entered Medline: 30 Nov 2004

ED Entered STN: 9 Oct 2004
Last Updated on STN: 19 Dec 2004
Entered Medline: 30 Nov 2004

AB BACKGROUND: The antimicrobial peptides human beta-defensin 1 and 2 (hBD-1 and 2) and the cathelicidin LL-37/hCAP-18 are key factors in innate immune responses of the respiratory tract. The aim of this study was to determine the concentrations of these peptides in airway surface fluid of CF patients with mild lung disease. METHODS: We measured the concentrations of hBD-1, hBD-2, and LL-37 in bronchoalveolar lavage fluid of 20 patients (5-34 years) participating in the prospective BEAT-study (bronchoalveolar lavage for the evaluation of anti-inflammatory treatment) using an immuno-dot blot-assay. RESULTS: All three peptides could be detected in lavage fluid of the study population. Increased levels of inflammatory markers in bronchoalveolar lavage fluid were associated with elevated concentrations of LL-37/hCAP-

18 (total cell count, P = 0.006; relative neutrophil count, P = 0.002). Deterioration of lung function, measured by MEF25 (maximal flow rate at 25% of residual forced vital capacity), correlated with decreased hBD-2 (P = 0.026), but increased LL-37/hCAP-18 concentrations (P = 0.016). CONCLUSIONS: The data suggest that concentrations of antimicrobial peptides are correlated with severity of CF lung disease: Levels of LL-37/hCAP-18 are associated with bronchial inflammation and, therefore disease severity, whereas decreased levels of beta-defensins in advanced lung disease likely contribute to a secondary defect of the local host defense.

L3 ANSWER 12 OF 36 MEDLINE on STN DUPLICATE 5
ACCESSION NUMBER: 2003238798 MEDLINE
DOCUMENT NUMBER: PubMed ID: 12600826
TITLE: The antimicrobial activity of the cathelicidin LL37 is inhibited by F-actin bundles and restored by gelsolin.
AUTHOR: Weiner Daniel J; Bucki Robert; Janmey Paul A
CORPORATE SOURCE: Division of Pulmonary Medicine, The Children's Hospital of Philadelphia, Philadelphia, Pennsylvania, USA.
CONTRACT NUMBER: HL67286 (NHLBI)
SOURCE: American journal of respiratory cell and molecular biology, (2003 Jun) Vol. 28, No. 6, pp. 738-45. Electronic Publication: 2002-12-30.
Journal code: 8917225. ISSN: 1044-1549.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200307
ENTRY DATE: Entered STN: 23 May 2003
Last Updated on STN: 11 Jul 2003
Entered Medline: 10 Jul 2003
ED Entered STN: 23 May 2003
Last Updated on STN: 11 Jul 2003
Entered Medline: 10 Jul 2003
AB Antimicrobial peptides are part of the innate host defense system, and inactivation of these peptides is implicated in airway infections in cystic fibrosis (CF). The sputum of patients with CF contains anionic polyelectrolytes, including F-actin and DNA not found in normal airway fluid. These anionic filaments aggregate to contribute to the altered viscoelastic properties of CF sputum. We hypothesized that the airway components stabilizing bundles of F-actin and DNA are in part cationic antimicrobial agents, and that appropriate modification of diseased airway fluid of patients with CF might dissociate these bundles and restore antimicrobial activity. We demonstrate that the human cathelicidin peptide LL37 forms bundles with F-actin and DNA, which are dissolved by gelsolin and DNase, respectively. Coincident with bundle formation, antimicrobial activity of LL37 is inhibited by F-actin and DNA. Pseudomonas bacteria were killed by low concentrations of LL37, but killing was significantly reduced in the presence of F-actin. The actin filament-fragmenting protein gelsolin restored bactericidal activity nearly completely. In a growth inhibition assay, the effects of F-actin were confirmed, and DNA was also shown to inhibit the activity of LL37. When added to CF sputum, gelsolin significantly reduced the growth of bacteria, suggesting activation of endogenous antimicrobial factors. These findings may have therapeutic implications for treatments previously thought to alter only the viscoelastic properties of airway secretions and amplify the possible advantage of gelsolin in CF treatment.

L3 ANSWER 13 OF 36 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2003:376066 BIOSIS

DOCUMENT NUMBER: PREV200300376066
TITLE: Inhibition of antimicrobial petides by exopolysaccharides of lung pathogens.
AUTHOR(S): Benincasa, M. [Reprint Author]; Mattiuzzo, M. [Reprint Author]; Herasimenka, Y. [Reprint Author]; Cescutti, P. [Reprint Author]; Rizzo, R. [Reprint Author]; Gennaro, R. [Reprint Author]
CORPORATE SOURCE: Department of Biochemistry, University of Trieste, I-34127, Trieste, Italy
SOURCE: Biopolymers, (2003) Vol. 71, No. 3, pp. 382-383. print.
Meeting Info.: 18th American Peptide Symposium on Peptide Revolution: Genomics, Proteomics and Therapeutics. Boston, MA, USA. July 19-23, 2003. American Peptide Society.
ISSN: 0006-3525 (ISSN print).
DOCUMENT TYPE: Conference; (Meeting)
Conference; (Meeting Poster)
Conference; Abstract; (Meeting Abstract)
LANGUAGE: English
ENTRY DATE: Entered STN: 13 Aug 2003
Last Updated on STN: 13 Aug 2003
ED Entered STN: 13 Aug 2003
Last Updated on STN: 13 Aug 2003

L3 ANSWER 14 OF 36 EMBASE
ACCESSION NUMBER: 2003368254 EMBASE
TITLE: [Antibiotic therapy against Pseudomonas aeruginosa and other gram-negative pathogens in cystic fibrosis].
TRAITEMENT ANTI-INFECTIEUX VIS-A-VIS DU PSEUDOMONAS AERUGINOSA ET AUTRES BACILLES A GRAM NEGATIF DANS LA MUCOVISCIDOSE.
AUTHOR: Le Bourgeois M.
CORPORATE SOURCE: M. Le Bourgeois, Serv. Pneumologie/Allergol. Pediat., Hopital Necker-Enfants-Malades, AP-HP, 149, rue de Sevres, 75015 Paris, France. muriel.lebourgeois@nck.ap-hop-paris.fr
SOURCE: Archives de Pediatrie, (1 Sep 2003) Vol. 10, No. SUPPL. 2, pp. 352s-357s. .
Refs: 36
ISSN: 0929-693X CODEN: APEDE4
COUNTRY: France
DOCUMENT TYPE: Journal; Conference Article
FILE SEGMENT: 004 Microbiology
007 Pediatrics and Pediatric Surgery
015 Chest Diseases, Thoracic Surgery and Tuberculosis
037 Drug Literature Index
LANGUAGE: French
SUMMARY LANGUAGE: English; French
ENTRY DATE: Entered STN: 2 Oct 2003
Last Updated on STN: 2 Oct 2003
ED Entered STN: 2 Oct 2003
Last Updated on STN: 2 Oct 2003
AB In cystic fibrosis patients, bronchial infection with Pseudomonas aeruginosa (PA) is frequent, occurring often early in life. It becomes chronic because of a particular relationship between bacteria and host. Intensive antibiotic treatment often permits a transient eradication. When infection becomes chronic, antibiotics must be prescribed in a way to afford resistance. Efficacy of nebulized antibiotics is now recognized. Problems persist. Because of the difficulty to eradicate PA, new strategies may consist in diminishing the pathogenicity of PA, by inhibiting adhesion and virulence factors' production. .COPYRGT. 2003 Elsevier SAS. Tous droits reserves.

L3 ANSWER 15 OF 36 EMBASE

ACCESSION NUMBER: 2003002198 EMBASE
TITLE: Molecular mechanisms in allergy and clinical immunology: Biology and clinical relevance of naturally occurring antimicrobial peptides.
AUTHOR: Gallo R.L.; Murakami M.; Ohtake T.; Zaiou M.
CORPORATE SOURCE: Dr. R.L. Gallo, 111B, 3350 LaJolla Village Drive, San Diego, CA 92161, United States
SOURCE: Journal of Allergy and Clinical Immunology, (1 Dec 2002) Vol. 110, No. 6, pp. 823-831. .
Refs: 99
ISSN: 0091-6749 CODEN: JACIBY
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 16 Jan 2003
Last Updated on STN: 16 Jan 2003
ED Entered STN: 16 Jan 2003
Last Updated on STN: 16 Jan 2003
AB Within the last decade, several peptides have been discovered on the basis of their ability to inhibit the growth of potential microbial pathogens. These so-called antimicrobial peptides participate in the innate immune response by providing a rapid first-line defense against infection. Recent advances in this field have shown that peptides belonging to the cathelicidin and defensin gene families are of particular importance to the mammalian immune defense system. This review discusses the biology of these molecules, with emphasis on their structure, processing, expression and function. Current evidence has shown that both cathelicidins and defensins are multifunctional and that they act both as natural antibiotics and as signaling molecules that activate host cell processes involved in immune defense and repair. The abnormal expression of these peptides has also been associated with human disease. Current and future studies are likely to implicate the presence of antimicrobial peptides in several unexplained human inflammatory disorders and to provide novel therapeutic approaches to the treatment of disease.

L3 ANSWER 16 OF 36 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 2002:233131 BIOSIS
DOCUMENT NUMBER: PREV200200233131
TITLE: Antimicrobial polypeptides in host defense of the respiratory tract.
AUTHOR(S): Ganz, Tomas [Reprint author]
CORPORATE SOURCE: Center for the Health Sciences, University of California-Los Angeles School of Medicine, 10833 LeConte Avenue, 37-055, Los Angeles, CA, 90095-1690, USA
tganz@ucla.edu
SOURCE: Journal of Clinical Investigation, (March, 2002) Vol. 109, No. 6, pp. 693-697. print.
CODEN: JCINAO. ISSN: 0021-9738.
DOCUMENT TYPE: Article
LANGUAGE: English
ENTRY DATE: Entered STN: 10 Apr 2002
Last Updated on STN: 10 Apr 2002
ED Entered STN: 10 Apr 2002
Last Updated on STN: 10 Apr 2002

L3 ANSWER 17 OF 36 MEDLINE on STN DUPLICATE 6
ACCESSION NUMBER: 2004022647 MEDLINE
DOCUMENT NUMBER: PubMed ID: 14720045
TITLE: The role of defensins in lung biology and therapy.
AUTHOR: Cole Alexander M; Waring Alan J
CORPORATE SOURCE: Department of Medicine, Division of Pulmonary and Critical Care Medicine,UCLA School of Medicine, Los Angeles,

California 90095, USA.. acole@mednet.ucla.edu
SOURCE: American journal of respiratory medicine : drugs, devices, and other interventions, (2002) Vol. 1, No. 4, pp. 249-59. Ref: 135
Journal code: 101132974. ISSN: 1175-6365.
PUB. COUNTRY: New Zealand
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200402
ENTRY DATE: Entered STN: 15 Jan 2004
Last Updated on STN: 7 Feb 2004
Entered Medline: 6 Feb 2004

ED Entered STN: 15 Jan 2004
Last Updated on STN: 7 Feb 2004
Entered Medline: 6 Feb 2004

AB Innate host defence, involving both cellular and humoral mediators, is a prominent function of the human airways. Cellular mediators of innate immunity include dendritic cells, natural killer cells, cytotoxic T cells, macrophages and neutrophils, while humoral mediators of innate immunity consist of components of the epithelial lining fluid (ELF) covering the airways. Microbicidal substances in the ELF can selectively disrupt bacterial cell walls and membranes, sequester microbial nutrients or act as decoys for microbial attachment. Antimicrobial components of airway secretions include lysozymes, lactoferrin, secretory leukoprotease inhibitor, defensins and cathelicidins. Defensins are the most widely studied family of antimicrobial peptides present in airway fluid. Humans produce at least 10 different defensin molecules, six alpha-defensins and four beta-defensins similar in structure and function. Direct evidence that defensins have central roles in host defense has only recently become available. Some defensins and defensin-like molecules could serve as templates for the development of pulmonary pharmaceuticals. As potential therapeutics, they possess several desirable properties, including the ability to kill a broad spectrum of micro-organisms while permitting little development of microbial resistance. Many peptides can also neutralize effects of lipopolysaccharide on macrophages and other host defense cells and decrease the release of proinflammatory cytokines thereby giving protection against septic shock. Protegrin-1 is a minidefensin isolated from pig leukocytes and has proved to be an attractive template for large-scale development of antibacterials. One such protegrin analog, iseganan is in phase III clinical trials for the treatment of oral mucositis secondary to systemic chemotherapy. Other prospective uses of iseganan include control of respiratory pathogens in patients with cystic fibrosis and reduction of oral bacteria to prevent ventilator-associated pneumonia. However, in order to advance the production and clinical testing of peptide-based therapeutics, technical hurdles of synthesizing large quantities of complexly folded peptides must be first overcome. Strategies to develop potent peptide-based microbicides are promising in the struggle against increasingly resistant pathogens.

L3 ANSWER 18 OF 36 MEDLINE on STN DUPLICATE 7
ACCESSION NUMBER: 2001509678 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11557478
TITLE: Cathelicidin peptides inhibit multiply antibiotic-resistant pathogens from patients with cystic fibrosis.
AUTHOR: Saiman L; Tabibi S; Starner T D; San Gabriel P; Winokur P L; Jia H P; McCray P B Jr; Tack B F
CORPORATE SOURCE: Department of Pediatrics, Columbia University, 650 West 168th St., New York, NY 10032, USA.. LS5@columbia.edu
CONTRACT NUMBER: HL 51670-05 (NHLBI)
HL-61234 (NHLBI)
P30 DK-97010 (NIDDK)

SOURCE: Antimicrobial agents and chemotherapy, (2001 Oct) Vol. 45, No. 10, pp. 2838-44.
Journal code: 0315061. ISSN: 0066-4804.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200112
ENTRY DATE: Entered STN: 17 Sep 2001
Last Updated on STN: 22 Jan 2002
Entered Medline: 4 Dec 2001

ED Entered STN: 17 Sep 2001
Last Updated on STN: 22 Jan 2002
Entered Medline: 4 Dec 2001

AB Endogenous peptide antibiotics are under investigation as inhaled therapeutic agents for cystic fibrosis (CF) lung disease. The bactericidal activities of five cathelicidin peptides (LL37 [human], CAP18 [rabbit], mCRAMP [mouse], rCRAMP [rat], and SMAP29 [sheep]), three novel alpha-helical peptides derived from SMAP29 and termed ovispirins (OV-1, OV-2, and OV-3), and two derivatives of CAP18 were tested by broth microdilution assays. Their MICs were determined for multiply antibiotic-resistant Pseudomonas aeruginosa (n = 24), Burkholderia cepacia (n = 5), Achromobacter xylosoxidans (n = 5), and Stenotrophomonas maltophilia (n = 5) strains isolated from CF patients. SMAP29 was most active and inhibited mucoid and nonmucoid P. aeruginosa strains (MIC, 0.06 to 8 microg/ml). OV-1, OV-2, and OV-3 were nearly as active (MIC, 0.03 to 16 microg/ml); but CAP18 (MIC, 1.0 to 32 microg/ml), CAP18 -18 (MIC, 1.0 to >32 microg/ml), and CAP18-22 (MIC, 0.5 to 32 microg/ml) had variable activities. LL37, mCRAMP, and rCRAMP were least active against the clinical isolates studied (MIC, 1.0 to >32 microg/ml). Peptides had modest activities against S. maltophilia and A. xylosoxidans (MIC range, 1.0 to > 32 microg/ml), but none inhibited B. cepacia. However, CF sputum inhibited the activity of SMAP29 substantially. The effects of peptides on bacterial cell membranes and eukaryotic cells were examined by scanning electron microscopy and by measuring transepithelial cell resistance, respectively. SMAP29 caused the appearance of bacterial membrane blebs within 1 min, killed P. aeruginosa within 1 h, and caused a dose-dependent, reversible decrease in transepithelial resistance within 5 h. The tested cathelicidin -derived peptides represent a novel class of antimicrobial agents and warrant further development as prophylactic or therapeutic agents for CF lung disease.

L3 ANSWER 19 OF 36 EMBASE
ACCESSION NUMBER: 2002164758 EMBASE
TITLE: Epithelial antimicrobial peptides and proteins: Their role in host defence and inflammation.
AUTHOR: Hiemstra P.S.
CORPORATE SOURCE: Dr. P.S. Hiemstra, Dept. of Pulmonology, Leiden University Medical Centre, Albinusdreef 2, 2300 RC Leiden, Netherlands. P.S.Hiemstra@lumc.nl
SOURCE: Paediatric Respiratory Reviews, (2001) Vol. 2, No. 4, pp. 306-310. .
Refs: 26
ISSN: 1526-0550 CODEN: PRRAEZ
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 007 Pediatrics and Pediatric Surgery
015 Chest Diseases, Thoracic Surgery and Tuberculosis
026 Immunology, Serology and Transplantation
030 Pharmacology
037 Drug Literature Index
LANGUAGE: English

SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 23 May 2002
Last Updated on STN: 23 May 2002
ED Entered STN: 23 May 2002
Last Updated on STN: 23 May 2002
AB Various antimicrobial mechanisms act in concert to protect the lung from infection by forming an efficient host defence system. Most microbial challenges are counteracted by elements of the innate immune system and antimicrobial peptides and proteins have been identified as key components of innate immunity. Although phagocytes are an important cellular source of these so-called endogenous antibiotics, it is now recognized that the airway epithelium is also a major site of synthesis. Antimicrobial peptides and proteins kill a wide variety of micro-organisms. Their importance is illustrated by the observation that in cystic fibrosis changes in the airway surface fluid may result in a dysfunction of these components. Recent studies have revealed other functions of these molecules showing they may link innate and adaptive immunity and appear to be involved in the regulation of inflammation and tissue repair. .COPYRGT. 2001 Harcourt Publishers Ltd.

L3 ANSWER 20 OF 36 EMBASE
ACCESSION NUMBER: 2002160605 EMBASE
TITLE: Host-bacterial interactions in the initiation of inflammation.
AUTHOR: Rastogi D.; Ratner A.J.; Prince A.
CORPORATE SOURCE: A. Prince, College of Physicians and Surgeons, Columbia University, 650 West 168th Street, New York, NY 10032, United States. asp7@columbia.edu
SOURCE: Paediatric Respiratory Reviews, (2001) Vol. 2, No. 3, pp. 245-252. .
Refs: 30
ISSN: 1526-0550 CODEN: PRRAEZ
COUNTRY: United Kingdom
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 004 Microbiology
007 Pediatrics and Pediatric Surgery
015 Chest Diseases, Thoracic Surgery and Tuberculosis
026 Immunology, Serology and Transplantation
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 16 May 2002
Last Updated on STN: 16 May 2002
ED Entered STN: 16 May 2002
Last Updated on STN: 16 May 2002
AB The respiratory epithelium provides both a physical and an immunological barrier to inhaled pathogens. In the normal host, innate defences prevent bacteria from activating inflammation by providing efficient muco-ciliary clearance and antimicrobial activity. Bacteria that persist in the airway lumen, as in cystic fibrosis, activate both the professional immune cells in the respiratory mucosa as well as the more abundant airway epithelial cells. As most of the bacteria become entrapped in airway mucin, shed bacterial products such as pili, flagella, peptidoglycan and lipopolysaccharide from lysed bacteria are likely to be the stimuli most important in activating epithelial signalling. The airway cells respond briskly to bacterial components through several signalling systems which activate epithelial expression of pro-inflammatory cytokines and chemokines. These signals recruit neutrophils to the airways where they eliminate the contaminating bacteria causing inflammation and the ensuing clinical signs of infection. .COPYRGT. 2001 Harcourt Publishers Ltd.

L3 ANSWER 21 OF 36 EMBASE
ACCESSION NUMBER: 2001066758 EMBASE

TITLE: Bacterial infections and inflammation in the lungs of cystic fibrosis patients.
AUTHOR: Conese M.; Assael B.M.
CORPORATE SOURCE: Dr. M. Conese, Inst. Exp. Treatm. Cystic Fibrosis, H. S. Raffaele Scientific Institute, Via Olgettina 58, 20132 Milan, Italy. conese.massimo@hsr.it
SOURCE: Pediatric Infectious Disease Journal, (2001) Vol. 20, No. 2, pp. 207-213. .
Refs: 60
ISSN: 0891-3668 CODEN: PIDJEV
COUNTRY: United States
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 005 General Pathology and Pathological Anatomy
015 Chest Diseases, Thoracic Surgery and Tuberculosis
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 8 Mar 2001
Last Updated on STN: 8 Mar 2001
ED Entered STN: 8 Mar 2001
Last Updated on STN: 8 Mar 2001
AB The aim of this review is to describe the role of respiratory epithelial cells in processes that contribute to the pathogenesis of lung disease in patients with cystic fibrosis.

L3 ANSWER 22 OF 36 MEDLINE on STN DUPLICATE 8
ACCESSION NUMBER: 2000231814 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10768969
TITLE: Bactericidal activity of mammalian cathelicidin -derived peptides.
AUTHOR: Travis S M; Anderson N N; Forsyth W R; Espiritu C; Conway B D; Greenberg E P; McCray P B Jr; Lehrer R I; Welsh M J; Tack B F
CORPORATE SOURCE: Department of Internal Medicine, University of Iowa College of Medicine Iowa City, Iowa 52242, USA.
CONTRACT NUMBER: AI29839 (NIAID)
AI43934 (NIAID)
HL61234 (NHLBI)
SOURCE: Infection and immunity, (2000 May) Vol. 68, No. 5, pp. 2748-55.
Journal code: 0246127. ISSN: 0019-9567.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200006
ENTRY DATE: Entered STN: 22 Jun 2000
Last Updated on STN: 16 Jul 2001
Entered Medline: 13 Jun 2000
ED Entered STN: 22 Jun 2000
Last Updated on STN: 16 Jul 2001
Entered Medline: 13 Jun 2000
AB Endogenous antimicrobial peptides of the cathelicidin family contribute to innate immunity. The emergence of widespread antibiotic resistance in many commonly encountered bacteria requires the search for new bactericidal agents with therapeutic potential. Solid-phase synthesis was employed to prepare linear antimicrobial peptides found in cathelicidins of five mammals: human (FALL39/ LL37), rabbit (CAP18), mouse (mCRAMP), rat (rCRAMP), and sheep (SMAP29 and SMAP34). These peptides were tested at ionic strengths of 25 and 175 mM against Pseudomonas aeruginosa, Escherichia coli, Staphylococcus aureus, and methicillin-resistant Staphylococcus aureus. Each peptide manifested activity against P. aeruginosa irrespective of the NaCl concentration. CAP18 and SMAP29 were the most effective peptides of the group against all test organisms under both low- and

high-salt conditions. Select peptides of 15 to 21 residues, modeled on CAP18 (37 residues), retained activity against the gram-negative bacteria and methicillin-sensitive S. aureus, although the bactericidal activity was reduced compared to that of the parent peptide. In accordance with the behavior of the parent molecule, the truncated peptides adopted an alpha-helical structure in the presence of trifluoroethanol or lipopolysaccharide. The relationship between the bactericidal activity and several physiochemical properties of the cathelicidins was examined. The activities of the full-length peptides correlated positively with a predicted gradient of hydrophobicity along the peptide backbone and with net positive charge; they correlated inversely with relative abundance of anionic residues. The salt-resistant, antimicrobial properties of CAP18 and SMAP29 suggest that these peptides or congeneric structures have potential for the treatment of bacterial infections in normal and immunocompromised persons and individuals with cystic fibrosis.

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ACCESSION NUMBER: 2000430967 EMBASE
TITLE: The treatment of respiratory pseudomonas infection in cystic fibrosis: What drug and which way?.
AUTHOR: Banerjee D.; Stableforth D.
CORPORATE SOURCE: Dr. D. Stableforth, Department of Respiratory Medicine, Birmingham Heartlands Hospital, Bordesley Green East, Birmingham B9 5SS, United Kingdom
SOURCE: Drugs, (2000) Vol. 60, No. 5, pp. 1053-1064. .
Refs: 58
ISSN: 0012-6667 CODEN: DRUGAY
COUNTRY: New Zealand
DOCUMENT TYPE: Journal; General Review
FILE SEGMENT: 004 Microbiology
015 Chest Diseases, Thoracic Surgery and Tuberculosis
030 Pharmacology
037 Drug Literature Index
038 Adverse Reactions Titles
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 5 Jan 2001
Last Updated on STN: 5 Jan 2001

ED Entered STN: 5 Jan 2001
Last Updated on STN: 5 Jan 2001

AB Pseudomonas aeruginosa is a non-capsulate and non-sporing Gram-negative bacillus that most commonly affects the lower respiratory system in humans. Burkholderia (previously Pseudomonas) cepacia has emerged as an important respiratory pathogen in patients with cystic fibrosis (CF). The ability of P. aeruginosa to persist and multiply in moist environments and equipment, such as humidifiers in hospital wards, bathrooms, sinks and kitchens, maybe of importance in cross-infection. P. aeruginosa infections of the lower respiratory tract can range in severity from colonisation (without an immunological response) to a severe necrotising bronchopneumonia. Infection is seen in patients with CF and other chronic lung diseases such as non-CF bronchiectasis. In patients with CF, once P. aeruginosa is established in the airways it is almost impossible to eradicate, but prior to this, aggressive treatment can delay the development of chronic infection. 30 to 40% of the present paediatric population with CF will have chronic pseudomonal infection. B. cepacia has a particular predisposition to infect patients with CF and may be distinguished from P. aeruginosa by accelerated lung disease in about one-third of patients. Overwhelming septicaemia and necrotising pneumonia are well described (cepacia syndrome); events that are rare with P. aeruginosa. With the propensity for social cross-infection, segregation policies have been accepted as means of controlling outbreaks. A number of antipseudomonal agents are

available. The most commonly used are the extended- spectrum penicillins, aminoglycosides, cephalosporins, fluoro-quinolones, polymixins and the monobactams. An aminoglycoside with a β-lactam penicillin is usually considered to be the first line treatment. No trial has shown any significant clinical advantage of any particular combination regimen over another. The emergence of resistance continues to be a concern. Pipericillin, piperacillin/tazobactam and meropenem have good but equivalent antibacterial activity against P. aeruginosa. However, B. cepacia is characterised by in vitro resistance to colistin (colomycin), aminoglycosides and ciprofloxacin but better susceptibility to ceftazidime. Nebulised delivery of antipseudomonal antibiotics is thought to prevent recurrent exacerbations, reduce antibiotic usage and maintain lung function, particularly in patients with CF. Colistin, tobramycin and gentamicin are currently the most commonly prescribed nebulised antibiotics. Much effort is directed at treating chronic P. aeruginosa infection but as chronic infection is seldom if ever eradicated when first established, prevention is preferable. Early intensive treatment for P. aeruginosa infection is advocated in order to maintain pulmonary function and postpone the onset of chronic P. aeruginosa infection.

L3 ANSWER 24 OF 36 MEDLINE on STN DUPLICATE 9
ACCESSION NUMBER: 2000505409 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11053013
TITLE: Synergistic and additive killing by antimicrobial factors found in human airway surface liquid.
AUTHOR: Singh P K; Tack B F; McCray P B Jr; Welsh M J
CORPORATE SOURCE: Department of Internal Medicine, University of Iowa College of Medicine, Iowa City, Iowa 52242, USA.
CONTRACT NUMBER: HL-61234 (NHLBI)
K08-HL-04173-01 (NHLBI)
SOURCE: American journal of physiology. Lung cellular and molecular physiology, (2000 Nov) Vol. 279, No. 5, pp. L799-805.
Journal code: 100901229. ISSN: 1040-0605.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200011
ENTRY DATE: Entered STN: 22 Mar 2001
Last Updated on STN: 22 Mar 2001
Entered Medline: 9 Nov 2000
ED Entered STN: 22 Mar 2001
Last Updated on STN: 22 Mar 2001
Entered Medline: 9 Nov 2000
AB Airway surface liquid contains multiple factors thought to provide a first line of defense against bacteria deposited in the airways. Although the antimicrobial action of individual factors has been studied, less is known about how they work in combination. We examined the combined action of six antimicrobial peptides found in airway surface liquid. The paired combinations of lysozyme-lactoferrin, lysozyme-secretory leukocyte protease inhibitor (SLPI), and lactoferrin-SLPI were synergistic. The triple combination of lysozyme, lactoferrin, and SLPI showed even greater synergy. Other combinations involving the human beta-defensins, LL-37, and tobramycin (often administered to cystic fibrosis patients by inhalation) were additive. Because the airway surface liquid salt concentration may be elevated in cystic fibrosis patients, we examined the effect of salt on the synergistic combinations. As the ionic strength increased, synergistic interactions were lost. Our data suggest that the antibacterial potency of airway surface liquid may be significantly increased by synergistic and additive interactions between antimicrobial factors. These results also suggest that increased salt concentrations that may exist in cystic fibrosis could inhibit airway defenses by diminishing these synergistic interactions.

L3 ANSWER 25 OF 36 MEDLINE on STN DUPLICATE 10
ACCESSION NUMBER: 2000477717 MEDLINE
DOCUMENT NUMBER: PubMed ID: 11028166
TITLE: [Antimicrobial peptides and peptide antibiotics]. Antimikrobielle Peptide und Peptidantibiotika.
AUTHOR: Bals R
CORPORATE SOURCE: Medizinische Klinik und Poliklinik I, Universitat Munchen, Grosshadern.. rbals@med1.med.uni-muenchen.de
SOURCE: Medizinische Klinik (Munich, Germany : 1983), (2000 Sep 15) Vol. 95, No. 9, pp. 496-502. Ref: 54
Journal code: 8303501. ISSN: 0723-5003.
PUB. COUNTRY: GERMANY: Germany, Federal Republic of
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: German
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200011
ENTRY DATE: Entered STN: 22 Mar 2001
Last Updated on STN: 22 Mar 2001
Entered Medline: 8 Nov 2000
ED Entered STN: 22 Mar 2001
Last Updated on STN: 22 Mar 2001
Entered Medline: 8 Nov 2000
AB Antimicrobial peptides are naturally occurring antibiotics. As part of the innate immune system of vertebrates they have direct antimicrobial function. Further, they can act as mediators of inflammation. Their antimicrobial spectrum covers gram-positive and -negative bacteria as well as fungi and certain viruses. Based on their structure, antimicrobial peptides can be divided into several families. Peptides of the defensin, cathelicidin, and histatin families have been isolated from humans, where they have been found in defense cells, such as macrophages or neutrophils, as well as in epithelial cells. Decreased production of antimicrobial peptides is associated with immune deficiencies. Further, lung disease in cystic fibrosis may be linked to the dysfunction of antimicrobial peptides. Based on naturally occurring antimicrobial peptides, derivates of these molecules were developed as innovative antibiotic drugs. The present review focuses on the biology of antimicrobial peptides as well as their potential as drugs.

L3 ANSWER 26 OF 36 EMBASE
ACCESSION NUMBER: 2000419116 EMBASE
TITLE: Synergistic and additive killing by antimicrobial factors found in human airway surface liquid.
AUTHOR: Singh P.K.; Tack B.F.; McCray P.B. Jr.; Welsh M.J.
CORPORATE SOURCE: M.J. Welsh, Howard Hughes Medical Institute, Univ. of Iowa College of Medicine, 500 EMRB, Iowa City, IA 52242, United States. mjwelsh@blue.weeg.uiowa.edu
SOURCE: American Journal of Physiology - Lung Cellular and Molecular Physiology, (2000) Vol. 279, No. 5 23-5, pp. L799-L805. .
Refs: 34
ISSN: 1040-0605 CODEN: APLPE7
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 002 Physiology
004 Microbiology
015 Chest Diseases, Thoracic Surgery and Tuberculosis
029 Clinical Biochemistry
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 14 Dec 2000
Last Updated on STN: 14 Dec 2000
ED Entered STN: 14 Dec 2000
Last Updated on STN: 14 Dec 2000

AB Airway surface liquid contains multiple factors thought to provide a first line of defense against bacteria deposited in the airways. Although the antimicrobial action of individual factors has been studied, less is known about how they work in combination. We examined the combined action of six antimicrobial peptides found in airway surface liquid. The paired combinations of lysozyme-lactoferrin, lysozyme-secretory leukocyte protease inhibitor (SLPI), and lactoferrin-SLPI were synergistic. The triple combination of lysozyme, lactoferrin, and SLPI showed even greater synergy. Other combinations involving the human β-defensins, LL-37, and tobramycin (often administered to cystic fibrosis patients by inhalation) were additive. Because the airway surface liquid salt concentration may be elevated in cystic fibrosis patients, we examined the effect of salt on the synergistic combinations. As the ionic strength increased, synergistic interactions were lost. Our data suggest that the antibacterial potency of airway surface liquid may be significantly increased by synergistic and additive interactions between antimicrobial factors. These results also suggest that increased salt concentrations that may exist in cystic fibrosis could inhibit airway defenses by diminishing these synergistic interactions.

L3 ANSWER 27 OF 36 MEDLINE on STN DUPLICATE 11
ACCESSION NUMBER: 1999225525 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10207162
TITLE: Transfer of a cathelicidin peptide antibiotic gene restores bacterial killing in a cystic fibrosis xenograft model.
AUTHOR: Bals R; Weiner D J; Meegalla R L; Wilson J M
CORPORATE SOURCE: Department of Medicine and Molecular and Cellular Engineering, Institute for Human Gene Therapy, The Wistar Institute, Philadelphia, Pennsylvania 19104-4268, USA.
CONTRACT NUMBER: P30 DK-47757 (NIDDK)
R01 HL-49040 (NHLBI)
SOURCE: The Journal of clinical investigation, (1999 Apr) Vol. 103, No. 8, pp. 1113-7.
Journal code: 7802877. ISSN: 0021-9738.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Abridged Index Medicus Journals; Priority Journals
ENTRY MONTH: 199905
ENTRY DATE: Entered STN: 14 Jun 1999
Last Updated on STN: 16 Jul 2001
Entered Medline: 28 May 1999

ED Entered STN: 14 Jun 1999
Last Updated on STN: 16 Jul 2001
Entered Medline: 28 May 1999

AB Recent studies suggest that the gene defect in cystic fibrosis (CF) leads to a breach in innate immunity. We describe a novel genetic strategy for reversing the CF-specific defect of antimicrobial activity by transferring a gene encoding a secreted cathelicidin peptide antibiotic into the airway epithelium grown in a human bronchial xenograft model. The airway surface fluid (ASF) from CF xenografts failed to kill Pseudomonas aeruginosa or Staphylococcus aureus. Partial reconstitution of CF transmembrane conductance regulator expression after adenovirus-mediated gene transfer restored the antimicrobial activity of ASF from CF xenografts to normal levels. Exposure of CF xenografts to an adenovirus expressing the human cathelicidin LL-37/hCAP-18 increased levels of this peptide in the ASF three- to fourfold above the normal concentrations, which were equivalent in ASF from CF and normal xenografts before gene transfer. The increase of LL-37 was sufficient to restore bacterial killing to normal levels. The data presented describe an alternative genetic approach to the treatment of CF based on enhanced expression of an endogenous antimicrobial peptide and

provide strong evidence that expression of antimicrobial peptides indeed protects against bacterial infection.

L3 ANSWER 28 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 2000:64903 CAPLUS
DOCUMENT NUMBER: 132:332293
TITLE: Physiology and pathology of tracheobronchial glands
AUTHOR(S): Finkbeiner, Walter E.
CORPORATE SOURCE: Department of Pathology, University of California, Sacramento, CA, 95817, USA
SOURCE: Respiration Physiology (1999), 118(2-3), 77-83
CODEN: RSPYAK; ISSN: 0034-5687
PUBLISHER: Elsevier Science Ireland Ltd.
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
ED Entered STN: 27 Jan 2000
AB A review, with 31 refs. The tracheobronchial glands, composed of mucous and serous secretory cells, provide a mucin-rich, antimicrobial-rich secretion for the conducting airways. The secretory processes of these cells are under complex neurohumoral control. Several diseases demonstrate considerable increases in the volume of secretory glands, the amount of glandular secretions or the character of the secretory product. The role of the tracheobronchial glands in the pathophysiol. of chronic bronchitis, asthma and cystic fibrosis is discussed.
REFERENCE COUNT: 32 THERE ARE 32 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 29 OF 36 MEDLINE on STN DUPLICATE 12
ACCESSION NUMBER: 2000086976 MEDLINE
DOCUMENT NUMBER: PubMed ID: 10618508
TITLE: Neutrophil antibacterial peptides, multifunctional effector molecules in the mammalian immune system.
AUTHOR: Gudmundsson G H; Agerberth B
CORPORATE SOURCE: Microbiology and Tumorbiology Center, Doktorsringen 13, Karolinska Institutet, S-171 77, Stockholm, Sweden.. gudmundur.gudmundsson@mtc.ki.se
SOURCE: Journal of immunological methods, (1999 Dec 17) Vol. 232, No. 1-2, pp. 45-54. Ref: 78
Journal code: 1305440. ISSN: 0022-1759.
PUB. COUNTRY: Netherlands
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 200001
ENTRY DATE: Entered STN: 4 Feb 2000
Last Updated on STN: 4 Feb 2000
Entered Medline: 21 Jan 2000
ED Entered STN: 4 Feb 2000
Last Updated on STN: 4 Feb 2000
Entered Medline: 21 Jan 2000
AB The bactericidal machinery of mammalian neutrophils is built up of many components with different chemical properties, involving proteins, peptides and oxygen-dependent radicals. All these components work in synergy, leading to destruction and elimination of ingested microbes. During the eighties, it gradually became clear, that cationic peptides are a part of the oxygen-independent bactericidal effectors in phagocytic cells. In mammals, these antimicrobial peptides are represented by two families, the defensins and the cathelicidins. These potent broad spectra peptides are included as immediate effector molecules in innate immunity. The detailed killing mechanism for these effectors is partly known, but nearly all of them have membrane affinity, and permeate bacterial membranes, resulting in lysis of the bacteria. This peptide-membrane interaction includes also eukaryotic membranes, that implicates cytotoxic effects on host cells. Studies in vitro have

established that the microenvironment is critical for their activities. In connection to cystic fibrosis, the effects of microenvironment changes are apparent, causing inactivation of peptide defences and leading to repeated serious bacterial infections. Thus, the importance of the microenvironment is also supported in vivo. Additional functions of these peptides such as chemotactic, mitogenic and stimulatory in the wound healing process suggest further important roles for these peptides.

L3 ANSWER 30 OF 36 CAPLUS COPYRIGHT 2007 ACS on STN
ACCESSION NUMBER: 1999:132402 CAPLUS
DOCUMENT NUMBER: 130:295175
TITLE: Antimicrobial peptides in mammalian and insect host defense
AUTHOR(S): Lehrer, Robert I.; Ganz, Tomas
CORPORATE SOURCE: Department of Medicine, The Molecular Biology Institute, UCLA School of Medicine, Los Angeles, CA, 90095, USA
SOURCE: Current Opinion in Immunology (1999), 11(1), 23-27
CODEN: COPIEL; ISSN: 0952-7915
PUBLISHER: Current Biology Publications
DOCUMENT TYPE: Journal; General Review
LANGUAGE: English
ED Entered STN: 02 Mar 1999
AB A review with 54 refs. During the past year, addnl. insights into systems that regulate antimicrobial peptide production in Drosophila were reported. Granulysin, a peptide stored in the cytoplasmic granules of human natural killer cells and cytolytic T cells, was shown to kill Mycobacterium tuberculosis. More data implicating antimicrobial peptides in the pathogenesis of bronchopulmonary infections in cystic fibrosis appeared. Studies that examined the potential contributions of antimicrobial peptides to regional innate immunity gained in prominence. Efforts to design peptide analogs to prevent or treat infections continued. Topics discussed include defensins, cathelicidins, protegrins, histatins, granulysin, secretory leukoprotease inhibitor, probiotics, and Drosophila antimicrobial peptides.
REFERENCE COUNT: 54 THERE ARE 54 CITED REFERENCES AVAILABLE FOR THIS RECORD. ALL CITATIONS AVAILABLE IN THE RE FORMAT

L3 ANSWER 31 OF 36 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 1999:324632 BIOSIS
DOCUMENT NUMBER: PREV199900324632
TITLE: Involvement of a protease in antimicrobial peptide resistance in Pseudomonas aeruginosa.
AUTHOR(S): Aspedon, A. [Reprint author]; Groisman, E. A.
CORPORATE SOURCE: Washington Univ. Sch. of Med., St. Louis, MO, USA
SOURCE: Abstracts of the General Meeting of the American Society for Microbiology, (1999) Vol. 99, pp. 14. print.
Meeting Info.: 99th General Meeting of the American Society for Microbiology. Chicago, Illinois, USA. May 30-June 3, 1999. American Society for Microbiology.
ISSN: 1060-2011.
DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)
LANGUAGE: English
ENTRY DATE: Entered STN: 24 Aug 1999
Last Updated on STN: 24 Aug 1999
ED Entered STN: 24 Aug 1999
Last Updated on STN: 24 Aug 1999

L3 ANSWER 32 OF 36 EMBASE COPYRIGHT (c) 2007 Elsevier B.V. All rights reserved on STN

ACCESSION NUMBER: 1998374307 EMBASE
TITLE: The peptide antibiotic LL-37/ hCAP-18 is expressed in epithelia of the human lung where it has broad antimicrobial activity at the airway surface.
AUTHOR: Bals R.; Wang X.; Zasloff M.; Wilson J.M.
CORPORATE SOURCE: J.M. Wilson, 204 Wistar Institute, 3601 Spruce Street, Philadelphia, PA 19104-4268, United States
SOURCE: Proceedings of the National Academy of Sciences of the United States of America, (4 Aug 1998) Vol. 95, No. 16, pp. 9541-9546. .
Refs: 36
ISSN: 0027-8424 CODEN: PNASA6
COUNTRY: United States
DOCUMENT TYPE: Journal; Article
FILE SEGMENT: 030 Pharmacology
037 Drug Literature Index
LANGUAGE: English
SUMMARY LANGUAGE: English
ENTRY DATE: Entered STN: 3 Dec 1998
Last Updated on STN: 3 Dec 1998
ED Entered STN: 3 Dec 1998
Last Updated on STN: 3 Dec 1998
AB The airway surface is an important host defense against pulmonary infection. Secretion of proteins with antimicrobial activity from epithelial cells onto the airway surface represents an important component of this innate immune system. Defensins are the best characterized epithelial- derived peptide antibiotics. A member of another family of peptide antibiotics called cathelicidins recently was identified from human bone marrow. We show in this paper that this human peptide named LL-37/hCAP-18 also may play a role in innate immunity of the human lung. In situ hybridization localized high levels of LL-37/hCAP-18 RNA to surface epithelial cells of the conducting airway as well as serous and mucous cells of the submucosal glands. LL-37/hCAP-18 peptide with antimicrobial activity was partially purified from airway surface fluid from human lung and a human bronchial xenograft model. The synthetic peptide LL-37 demonstrated antibiotic activity against a number of Gram-negative and Gram-positive organisms including Pseudomonas aeruginosa; bacterial killing of LL-37 was sensitive to NaCl and was synergistic with lactoferrin and lysozyme. In summary, we show that LL-37/hCAP-18 is a peptide with broad antimicrobial activity that is secreted onto the airway surface from epithelial cells of the human lung.

L3 ANSWER 33 OF 36 MEDLINE on STN DUPLICATE 13
ACCESSION NUMBER: 1998409704 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9736536
TITLE: Activities of LL-37, a cathelin-associated antimicrobial peptide of human neutrophils.
AUTHOR: Turner J; Cho Y; Dinh N N; Waring A J; Lehrer R I
CORPORATE SOURCE: Department of Medicine, Center for the Health Sciences, Los Angeles, California, USA.
CONTRACT NUMBER: AI 22839 (NIAID)
AI 37945 (NIAID)
HL 46809 (NHLBI)
SOURCE: Antimicrobial agents and chemotherapy, (1998 Sep) Vol. 42, No. 9, pp. 2206-14.
Journal code: 0315061. ISSN: 0066-4804.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
LANGUAGE: English
FILE SEGMENT: Priority Journals

ENTRY MONTH: 199810
ENTRY DATE: Entered STN: 29 Oct 1998
Last Updated on STN: 29 Oct 1998
Entered Medline: 22 Oct 1998
ED Entered STN: 29 Oct 1998
Last Updated on STN: 29 Oct 1998
Entered Medline: 22 Oct 1998
AB Human neutrophils contain two structurally distinct types of antimicrobial peptides, beta-sheet defensins (HNP-1 to HNP-4) and the alpha-helical peptide LL-37. We used radial diffusion assays and an improved National Committee for Clinical Laboratory Standards-type broth microdilution assay to compare the antimicrobial properties of LL -37, HNP-1, and protegrin (PG-1). Although generally less potent than PG-1, LL-37 showed considerable activity (MIC, <10 microgram/ml) against Pseudomonas aeruginosa, Salmonella typhimurium, Escherichia coli, Listeria monocytogenes, Staphylococcus epidermidis, Staphylococcus aureus, and vancomycin-resistant enterococci, even in media that contained 100 mM NaCl. Certain organisms (methicillin-resistant S. aureus, Proteus mirabilis, and Candida albicans) were resistant to LL-37 in media that contained 100 mM NaCl but were susceptible in low-salt media. Burkholderia cepacia was resistant to LL-37, PG-1, and HNP-1 in low- or high-salt media. LL-37 caused outer and inner membrane permeabilization of E. coli ML-35p. Chromogenic Limulus assays revealed that LL-37 bound to E. coli O111:B4 lipopolysaccharide (LPS) with a high affinity and that this binding showed positive cooperativity (Hill coefficient = 2.02). Circular dichroism spectrometry disclosed that LL-37 underwent conformational change in the presence of lipid A, transitioning from a random coil to an alpha-helical structure. The broad-spectrum antimicrobial properties of LL-37, its presence in neutrophils, and its inducibility in keratinocytes all suggest that this peptide and its precursor (hCAP-18) may protect skin and other tissues from bacterial intrusions and LPS-induced toxicity. The potent activity of LL-37 against P. aeruginosa, including mucoid and antibiotic-resistant strains, suggests that it or related molecules might have utility as topical bronchopulmonary microbicides in cystic fibrosis.

L3 ANSWER 34 OF 36 MEDLINE on STN DUPLICATE 14
ACCESSION NUMBER: 1999042660 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9825219
TITLE: Epithelial antimicrobial peptides: review and significance for oral applications.
AUTHOR: Weinberg A; Krisanaprakornkit S; Dale B A
CORPORATE SOURCE: Department of Periodontics, Case Western Reserve University, Cleveland, Ohio 44106-4905, USA.
CONTRACT NUMBER: DE 10329 (NIDCR)
SOURCE: Critical reviews in oral biology and medicine : an official publication of the American Association of Oral Biologists, (1998) Vol. 9, No. 4, pp. 399-414. Ref: 94
Journal code: 9009999. ISSN: 1045-4411.
PUB. COUNTRY: United States
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Dental Journals; Priority Journals
ENTRY MONTH: 199901
ENTRY DATE: Entered STN: 2 Feb 1999
Last Updated on STN: 3 Mar 2000
Entered Medline: 19 Jan 1999
ED Entered STN: 2 Feb 1999
Last Updated on STN: 3 Mar 2000
Entered Medline: 19 Jan 1999
AB Epithelial tissues provide the first line of defense between an organism

and the environment. Disruption of this barrier leads to bacterial invasion and subsequent inflammation. This is precisely the situation existing in the human oral cavity, where tissues are constantly exposed to a variety of microbial challenges that can lead to bacterially induced periodontal diseases, and to infections of the oral mucosa by bacteria, fungi, and viruses. With the recent discoveries of host-derived peptide antibiotics in mammalian mucosal epithelium, a new line of investigation is emerging to test the hypothesis that one class of these peptides, called "beta-defensins", functions to protect the host against microbial pathogenesis at these critical, confrontational sites. In that light, impairment of beta-defensin activity has recently been implicated in chronic bacterial infections in cystic fibrosis patients. The first direct evidence of expression of defensin peptides in the oral mucosa was the identification of a novel epithelial beta-defensin in mammalian tongue. It was shown to be upregulated in inflammation, suggesting that it participates in host defense. It is theorized that epithelial cell-derived antimicrobial peptides function to keep the natural flora of micro-organisms in a steady state in different niches such as the skin, the intestines, the airway, the endocervix, and the mouth. There is now evidence indicating that normal gingival epithelial cells and tissues express two beta-defensins, hBD-1 and the newly described hBD-2. In addition, a cathelin-class antimicrobial peptide, designated LL-37 and found in human neutrophils, is also expressed in skin and gingiva. It is highly likely that these and/or other epithelial antimicrobial peptides play an important role in determining the outcome of the host-pathogen interaction at the oral mucosal barrier, and that they may have important future applications in antibiotic treatment.

L3 ANSWER 35 OF 36 MEDLINE on STN DUPLICATE 15
ACCESSION NUMBER: 1998183710 MEDLINE
DOCUMENT NUMBER: PubMed ID: 9523109
TITLE: Antimicrobial peptides of vertebrates.
AUTHOR: Ganz T; Lehrer R I
CORPORATE SOURCE: Department of Medicine, University of California School of Medicine, Los Angeles 90095-1690, USA.. tganz@ucla.edu
SOURCE: Current opinion in immunology, (1998 Feb) Vol. 10, No. 1, pp. 41-4. Ref: 50
Journal code: 8900118. ISSN: 0952-7915.
PUB. COUNTRY: ENGLAND: United Kingdom
DOCUMENT TYPE: Journal; Article; (JOURNAL ARTICLE)
General Review; (REVIEW)
LANGUAGE: English
FILE SEGMENT: Priority Journals
ENTRY MONTH: 199805
ENTRY DATE: Entered STN: 9 Jun 1998
Last Updated on STN: 16 Jul 2001.
Entered Medline: 22 May 1998
ED Entered STN: 9 Jun 1998
Last Updated on STN: 16 Jul 2001
Entered Medline: 22 May 1998
AB The past year brought several discoveries that focused attention on antimicrobial peptides on epithelial surfaces. The malfunction of these substances was implicated as a cause of airway infections in cystic fibrosis. Other highlights included new insights into the relative selectivity of antimicrobial peptides for microbial membranes, their primary site of action.

L3 ANSWER 36 OF 36 BIOSIS COPYRIGHT (c) 2007 The Thomson Corporation on STN
ACCESSION NUMBER: 1997:241753 BIOSIS
DOCUMENT NUMBER: PREV199799540956
TITLE: Identification and analysis of a novel antibacterial factor in human airway surface fluid.
AUTHOR(S): Travis, S. M. [Reprint author]; Conway, B. A.; Smith, J.

J.; Greenberg, E. P.; Welsh, M. J.

CORPORATE SOURCE: HHMI, Dep. Internal Med., Univ. Iowa Coll. Med., Iowa City, IA 52242, USA

SOURCE: Journal of Investigative Medicine, (1997) Vol. 45, No. 3, pp. 287A.
Meeting Info.: Annual Meeting of the Association of American Physicians, the American Society for Clinical Investigation, and the American Federation for Medical Research: Biomedicine '97 Medical Research from Bench to Bedside. Washington, D.C., USA. April 25-27, 1997.
ISSN: 1081-5589.

DOCUMENT TYPE: Conference; (Meeting)
Conference; Abstract; (Meeting Abstract)
Conference; (Meeting Poster)

LANGUAGE: English

ENTRY DATE: Entered STN: 2 Jun 1997
Last Updated on STN: 2 Jun 1997

ED Entered STN: 2 Jun 1997
Last Updated on STN: 2 Jun 1997

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1: Laube DM, Yim S, Ryan LK, Kisich KO, Diamond G. Related Articles, Links

Antimicrobial peptides in the airway.
Curr Top Microbiol Immunol. 2006;306:153-82. Review.
PMID: 16909921 [PubMed - indexed for MEDLINE]

2: Agerberth B, Gudmundsson GH. Related Articles, Links

Host antimicrobial defence peptides in human disease.
Curr Top Microbiol Immunol. 2006;306:67-90. Review.
PMID: 16909918 [PubMed - indexed for MEDLINE]

3: Xiao W, Hsu YP, Ishizaka A, Kirikae T, Moss RB. Related Articles, Links

Sputum cathelicidin, urokinase plasminogen activation system components, and cytokines discriminate cystic fibrosis, COPD, and asthma inflammation.
Chest. 2005 Oct;128(4):2316-26.
PMID: 16236890 [PubMed - indexed for MEDLINE]

4: Chen CI, Schaller-Bals S, Paul KP, Wahn U, Bals R. Related Articles, Links

Beta-defensins and LL-37 in bronchoalveolar lavage fluid of patients with cystic fibrosis.
J Cyst Fibros. 2004 Mar;3(1):45-50.
PMID: 15463886 [PubMed - indexed for MEDLINE]

5: Weiner DJ, Bucki R, Janmey PA. Related Articles, Links

The antimicrobial activity of the cathelicidin LL37 is inhibited by F-actin bundles and restored by gelsolin.
Am J Respir Cell Mol Biol. 2003 Jun;28(6):738-45. Epub 2002 Dec 30.
PMID: 12600826 [PubMed - indexed for MEDLINE]

6: Saiman L, Tabibi S, Starner TD, San Gabriel P, Winokur PL, Jia HP, McCray PB Jr, Tack BF. Related Articles, Links

Cathelicidin peptides inhibit multiply antibiotic-resistant pathogens from patients with cystic fibrosis.
Antimicrob Agents Chemother. 2001 Oct;45(10):2838-44.
PMID: 11557478 [PubMed - indexed for MEDLINE]

7: Bals R. Related Articles, Links

[Antimicrobial peptides and peptide antibiotics]
Med Klin (Munich). 2000 Sep 15;95(9):496-502. Review. German.
PMID: 11028166 [PubMed - indexed for MEDLINE]

☐ **8:** Bals R, Weiner DJ, Meegalla RL, Wilson JM. Related Articles, Links

Transfer of a cathelicidin peptide antibiotic gene restores bacterial killing in a cystic fibrosis xenograft model.
J Clin Invest. 1999 Apr;103(8):1113-7.
PMID: 10207162 [PubMed - indexed for MEDLINE]

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#16	Search **smith jj travis sm**	12:46:55	2
#6	Search **"Cystic Fibrosis"[MeSH] OR "cystic lung fibrosis"**	11:53:49	21084
#3	Search **cathelicidin OR cap18 OR cap-18 OR hcap18 OR hcap-18 OR "cap 18" OR "hcap 18" OR fall39 OR fall-39 OR ll37 OR ll-37**	11:52:58	478

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